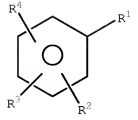
REMARKS

Claims 1-10, 12-13 and 15-60 are currently pending. Claims 5, 12-13 and 26-60 have been withdrawn. No claims have been amended. Applicants respectfully request reconsideration and allowance of all pending claims.

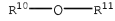
1. Rejection of Claims 1-4, 6-10, and 15-25 Under 35 U.S.C. § 103(a)

Reconsideration is requested of the rejection of claims 1-4, 6-10, and 15-25 under 35 U.S.C. § 103(a) as being unpatentable over Robbins, et al. (J. Clin. Microbiol. 1987) and Lambert (J. Applied Microbiol.) in view of Syverson (U.S. 5,612,045) or Syverson in view of Robbins, et al. and Lambert.

Claim 1 is directed to an exoprotein inhibitor for inhibiting the production of exoproteins from Gram positive bacteria in and around the vagina. The exoprotein inhibitor comprises a **non-absorbent substrate for insertion into a vagina being selected from the group consisting of a non-absorbent incontinence device, a barrier birth control device, a tampon applicator, and a douche.** The non-absorbent substrate has deposited thereon an effective amount of a first active ingredient and **an effective amount of a second active ingredient.** The first active ingredient has the general formula:



wherein R^1 is $-OR^6OH$; R^6 is a divalent saturated or unsaturated aliphatic hydrocarbyl moiety; R^2, R^3, and R^4 are independently selected from the group consisting of H, OH, COOH, and $-C(O)R^9$; R^9 is hydrogen or a monovalent saturated or unsaturated aliphatic hydrocarbyl moiety. The second active ingredient has the general formula:



wherein R^{10} is a straight or branched alkyl or straight or branched alkenyl having from 8 to about 18 carbon atoms and R^{11} is selected from the group consisting of an alcohol, a polyalkoxylated sulfate salt and a polyalkoxylated sulfosuccinate salt. Both the first active ingredient and second active ingredient are effective in inhibiting the production of exoprotein from Gram positive bacteria.

Robbins et al. disclose an analysis of the influence of 17 commercially available tampons on the production of toxic shock syndrome toxin 1 (TSST-1) by *S. aureus* using a tampon disk method. Specifically, a disk containing 10-ml of agar medium was overlaid with a Gelman GN-6 0.45-µm filter membrane and spread inoculated with 0.05 ml of an overnight still culture of *S. aureus* FRI-1169. In some samples, 10% blood was added to the agar medium. The test tampon was laid on the membrane and gently pressed down for uniform contact with the inoculated

membrane. The disk was then sealed and incubated at 37°C for 19 hours. A plate count agar was used for enumeration of colonies in the tampon and membrane and a single gel diffusion tube method was used to determine the toxin content of the agar layer under the tampon and membrane. It was found that the amount of toxin produced increased with all tampons when blood was added to the agar medium, with an average of 42% over that without the addition of blood. Robbins et al. teach that one function of tampons may be to support the vaginal infection by supplying a fibrous surface for heavy colonization and to provide a sufficiently aerobic environment for toxin production.

Robbins et al. further disclose the effect of tampon additives such as Aqualon, a surfactant, and a deodorant used in tampon manufacturing, on the growth of and TSST-1 production by *S. aureus*. It was found that the presence of the Aqualon in the tampons had little or **no effect on growth and TSST-1 production** by the *S. aureus* strain.[1] It was further shown, however, that when using the surfactant/deodorant-containing tampons, there was a >50% decrease in the amount of TSST-1 recovered from both the agar layer and the tampon disk.[2]

Lambert discloses a method of examining the effect of inoculum size on the degree of inhibition observed with respect to inhibitor concentration. Specifically, the inoculum size dependencies of phenethyl alcohol, phenoxyethanol, *p*-chloro-*m*-cresol, trichloro-phenol, thymol, and dodecyltrimethylammonium bromide against *S. aureus* were analyzed. For some inhibitors examined, such as dodecyltrimethylammonium bromide ($C1_2$QAC), it

[1] Robbins, et al. on page 1448.
[2] *Id.* at page 1449.

was found that at lower inoculum levels, there was a greater biocidal effect, whereas at higher inoculum levels, there was a greater degree of quenching of the biocide, causing the inhibitor to act more as a simple (sublethal) inhibitor. Lambert states that the method disclosed therein may be used to quantify the effect in the region between reversible and irreversible damage, or sublethal injury to cell death. Furthermore, Lambert states that the disclosed model suggests that on a molar basis, phenethyl alcohol is a better inhibitor than phenoxyethanol against *S. aureus*.

Both Robbins et al. and Lambert fail to disclose the use of phenoxyethanol (or any compound having the structure of the first active ingredient) in combination with a second active ingredient **on a non-absorbent substrate being selected from the group consisting of a non-absorbent incontinence device, a barrier birth control device, a tampon applicator, and a douche for insertion into the vagina** for inhibiting exoproteins from Gram positive bacteria as required in claim 1. Specifically, a second active ingredient having the structure as required in claim 1 was **never even mentioned** in the cited references. In an attempt to find each and every element of claim 1 as required by the M.P.E.P. for a determination of *prima facie* obviousness, the Office cites the Syverson reference for combination with Robbins et al. and Lambert.

Syverson is merely directed to **absorbent** articles, such as catamenial tampons, which include an effective amount of an ether compound to substantially inhibit the production of exotoxins by Gram positive bacteria. Moreover, nowhere in

Syverson is a first active ingredient as set forth in claim 1 even mentioned, much less that such a compound is effective in inhibiting the production of exoprotein from Gram positive bacteria when deposited on a non-absorbent substrate selected from the group consisting of a non-absorbent incontinence device, a barrier birth control device, a tampon applicator, and a douche. Accordingly, Syverson does not describe or suggest a non-absorbent substrate selected from the group consisting of a non-absorbent incontinence device, a barrier birth control device, a tampon applicator, and a douche.

In order for the Office to show a prima facie case of obviousness, M.P.E.P. § 2142 requires a clear articulation of the reasons why the claimed invention would have been obvious. Specifically, the Supreme Court in KSR International Co. v. Teleflex Inc., 550 U.S. 398, 82 USPQ2d 1385, 1396 (2007) noted that the burden lies initially with the Office to provide an explicit analysis supporting a rejection under 35 U.S.C. 103. "[R]ejections on obviousness cannot be sustained with mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." The Court in KSR International further identified a number of rationales to support a conclusion of obviousness which are consistent with the proper "functional approach" to the determination of obviousness as laid down in Graham v. John Deere Co. (383 U.S. 1, 148 USPQ 459 (1966). Specifically, as previously required by the TSM (teaching, suggestion, motivation) approach to obviousness, one exemplary rationale indicated requires some teaching, suggestion, or motivation in the prior art reference that would

have led one of ordinary skill to modify the prior art reference to arrive at the claimed invention.

Specifically, to reject a claim based on this rationale, the Office must articulate the following: (1) a finding that there was some teaching, suggestion, or motivation, either in the reference itself or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings to arrive at each and every limitation of the claimed invention; (2) a finding that there was reasonable expectation of success; and (3) whatever additional findings based on the Graham factual inquiries may be necessary, in view of the facts of the case under consideration, to explain a conclusion of obviousness. The Office has failed to meet its burden under number (1) above, as the cited references fail to show each and every limitation of Applicants' invention and there is no apparent reason for one skilled in the art to combine the reference teachings to arrive at each and every limitation. It simply would not have been obvious to one skilled in the art to arrive at Applicants' claimed combinations.

Specifically, as noted above, none of the cited references teach the use of a combination of a first active ingredient and a second active ingredient **on a non-absorbent substrate** for inhibiting exoprotein production. Nor do any of the cited references disclose or suggest any of the specific non-absorbent substrates listed in claim 1, i.e., non-absorbent incontinence device, a barrier birth control device, a tampon applicator, and

a douche. This element is entirely lacking from the cited references.

In the Response to Arguments section of the current Office action, the Office states that Syverson teaches both absorbent and non-absorbent articles with *S. aureus* exoprotein inhibiting compounds. Specifically, the Office states, citing to Syverson at column 3, lines 50-60, that tampons may be absorbent or non-absorbent. With all due respect, Applicants re-assert, for the reasons set forth in the previously submitted Amendment B and Response After RCE, that the Office is misconstruing the reference.

In particular, although Syverson discloses at column 3, lines 58-60, that "the tampon may be made of various fiber blends including **both absorbent and non-absorbent** fibers," (emphasis added) Syverson does not disclose that the tampon itself is non-absorbent. A person having ordinary skill in the art would readily understand that simply because an absorbent article may include a non-absorbent feature or fiber does not mean that the entire article is a non-absorbent article.[3] Applicants note that as stated in M.P.E.P. § 2141.02, "[A] prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention."[4] Furthermore,

[3] For example, a diaper, which is understood by a person having ordinary skill in the art to be an absorbent article, may have a non-absorbent feature (such as a water impermeable backsheet), while still remaining an absorbent article.

[4] M.P.E.P. § 2141.02 (emphasis in original) (citing W.L. Gore & Associates, Inc. v. Garlock, Inc., 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983)).

> [i]t is impermissible within the framework of section 103 to pick and choose from any one reference only so much of it as will support a given position, to the exclusion of other parts necessary to the full appreciation of what such references fairly suggests to one of ordinary skill in the art.[5]

Thus, reading and interpreting only a portion of a disclosure is inconsistent with M.P.E.P. rules. Syverson must thus be read as a whole, taking into consideration those portions that teach away from the claimed non-absorbent substrates, specifically, the teaching in Syverson that a tampon is an **absorbent** article, that may include a portion of non-absorbent fibers. In fact, the tampon, as described in Syverson, would not be effective for its intended use if the assembled tampon was non-absorbent. Further, a tampon, as defined in Merriam-Webster's Online Dictionary, is, "a wad of **absorbent material** introduced into a body cavity or canal usually to absorb secretions or to arrest hemorrhaging,"[6] (emphasis added).[7] As such, Applicants submit that one skilled in the art would readily understand that a catamenial tampon, as disclosed in Syverson, is **not** a non-absorbent substrate, as required by Applicants' claim 1.

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[5] Chisum § 5.03[3][a][i][F], quoting In re Wesslau, 353 F.2d 238, 241, 147 USPQ 391, 393 (CCPA 1965)). *See also id.* At n. 42 ("It is not permissible to pick and choose only so much of any given reference as will support a given position and ignore the reference in its totality." (quoting Lubrizol Corp. v. Exxon Corp., 696 F.Supp. 302, 322, 7 USPQ2d 1513, 1527 (N.D. Ohio 1988))).

[6] *See* http://www.merriam-webster.com/dictionary/tampon. A printout of this website is provided in a supplemental IDS submitted herewith.

[7] *See also* U.S. Patent Nos. 6,863,664 and 5,217,444, copies of which are submitted in a supplemental IDS filed herewith, for further evidence that one having ordinary skill in the art would readily understand that a tampon is an absorbent article.

Moreover, in the current Office Action, the Office states that Applicants' claim 1 "[N]owhere states that the substrate as well as fibers that make up the substrate is non-absorbent," and that the "comprising" language in Applicants' claim 1 "allows for the presence of absorbent fibers". Applicants respectfully disagree with the Office's position. In paragraph [0020] of the instant application, Applicants define the phrase "non-absorbent article" to generally refer to "[S]ubstrates or devices which include an outer layer formed from a substantially hydrophobic material which **repels fluids** such as menses, blood products and the like." (emphasis added) As the non-absorbent substrates "repel fluids," by their very nature they are not absorbent. Tampons, such as the catamenial tampon used in Syverson, on the other hand, absorb fluids such as menses and blood products. A person having ordinary skill in the art would readily ascertain this difference.

Furthermore, although the Office is correct in indicating that the term "comprising" is open-ended, and does not specifically exclude the presence of absorbent fibers in the substrate, applicants again point out that claim 1 requires the substrate itself to be a non-absorbent substrate. This is an explicit limitation in claim 1 and cannot be ignored. Thus, even if the substrate did contain some absorbent fibers, the substrate itself must be non-absorbent. One skilled in the art would clearly understand claim 1 to require non-absorbent substrates, given the above-recited definition of a non-absorbent article and the explicit recitation in claim 1 that the substrate is a non-absorbent substrate.

Further, applicants note that even if one having ordinary skill in the art interpreted the tampon of Syverson to be non-absorbent (which, Applicants submit one clearly would not do), Syverson, either alone or in combination with the cited references, still fails to disclose any of the non-absorbent substrates listed in Applicants' claim 1, i.e., a non-absorbent incontinence device, a barrier birth control device, a tampon applicator, or a douche. As noted above, this element of applicants' claim 1 is entirely lacking from the cited references.

Nor is there any apparent reason to modify the cited references to arrive at Applicants' claim 1. As recognized by the Supreme Court in KSR International Co. v. Teleflex, Inc., while an obviousness determination is not a rigid formula, the TSM (teaching, suggestion, motivation) test captures a helpful insight: "A patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art. Although common sense directs [caution as to] a patent application that claims as innovation the combination of two known [elements] according to their established functions, it can be important to identify a reason that would have prompted a person of ordinary skill in the [art] to combine the elements in the way the claimed new invention does."[8]

In the instant case, the common sense of one ordinarily skilled in the art would not have provided a reason to combine or modify the cited references to arrive at Applicants'

exoprotein inhibitor comprising a first active ingredient and a second active ingredient having the structures as required in claim 1 deposited on a non-absorbent substrate. For instance, it would not have been obvious to use the ether compounds of Syverson (which disclose absorbent articles) with a non-absorbent substrate, such as disclosed in the instant application. Specifically, as discussed above, absorbent and non-absorbent substrates have inherently different properties, and there is nothing in any of the cited references to suggest that the compounds of Syverson would be effective if used with a non-absorbent substrate. For instance, in the instant application, paragraph [0014] provides an example of how a non-absorbent substrate (e.g., tampon applicator) differs from an absorbent article such as a tampon. Specifically, the non-absorbent tampon applicator, which may have deposited thereon the claimed first and second active ingredients, houses the absorbent tampon. When the applicator is introduced into a woman's vaginal cavity, the first and second active ingredients are transferred from the non-absorbent applicator onto the wall of the vagina. The non-absorbent applicator is then removed from the cavity while the absorbent tampon remains in the cavity to absorb fluids. Thus, it would not be obvious to one having ordinary skill in the art to modify the teachings of the cited references to arrive at the non-absorbent substrates of Applicants' claim 1.

Furthermore, applicants submit that there is no apparent reason to combine the phenoxyethanol of Lambert with the ether

[8] 2007 WL at 5.

compounds of Syverson on a non-absorbent substrate. At best, Robbins et al. teach that the use of a surfactant or deodorant during the manufacturing of a tampon may inhibit exoprotein production and growth of *S. aureus*. Nowhere, however, is phenoxyethanol or the second active ingredient having the structure set forth in claim 1 even mentioned. Furthermore, while Lambert does analyze phenoxyethanol as one of six inhibitors that may inhibit exoprotein production, Lambert fails to teach or suggest the use of a second active ingredient with the phenoxyethanol to inhibit exoprotein production. In particular, no second active ingredient, either having the structure as required in claim 1 or otherwise, is even mentioned in Lambert. Thus, even if one skilled in the art did select phenoxyethanol as the first active ingredient based on the teachings of Lambert, there is nothing in the cited references to motivate one to also include a second active ingredient, much less the specific second active ingredient of claim 1. Moreover, why would one skilled in the art be motivated to add the second active ingredient of claim 1 when Lambert teaches that phenoxyethanol already inhibits the exoprotein production? Based on the teachings of the cited references, there is simply no motivation to combine the cited references to arrive at Applicants' instant claim 1.

As none of the cited references teach or suggest using the first active ingredient and second active ingredient having the structures as set forth in claim 1 on a non-absorbent substrate selected from the group consisting of a non-absorbent incontinence device, a barrier birth control device, a tampon

applicator, and a douche for insertion into the vagina for inhibiting exoproteins from Gram positive bacteria, claim 1 is patentable over the combination of Robbins et al., Lambert, and Syverson.

Claims 2-4, 6-10, and 15-25 depend directly or indirectly on claim 1. As such, claims 2-4, 6-10, and 15-25 are patentable over the cited references for the same reasons as claim 1 set forth above, as well as for the additional elements they require.

CONCLUSION

In view of the above, Applicants respectfully request favorable reconsideration and allowance of all pending claims. The Commissioner is hereby authorized to charge any fee deficiency in connection with this Response to Office Action to Deposit Account Number 01-2384.

Respectfully Submitted,

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